



## EDITORIAL COMMENT

# A new look at the prevalence of atrial fibrillation in Portugal: The Safira study<sup>☆</sup>



## Um novo olhar sobre a prevalência da fibrilhação auricular em Portugal – O Estudo Safira

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Atrial fibrillation (AF) is the most common sustained arrhythmia in clinical practice and is a significant cause of morbidity, mainly due to the associated risk of ischemic stroke.<sup>1</sup> It is thus an independent risk factor for cardiac mortality. As AF is directly associated with age, the number of patients with AF is expected to grow exponentially in the coming decades as the population ages.<sup>2</sup>

It is thus crucial to know the prevalence of AF, in order to optimize cardiovascular health strategies, especially since the incidence of stroke and the associated mortality rate are very high in Portugal compared to other European Union countries.<sup>3</sup>

The incidence and prevalence of AF have been estimated in several studies published since the 1980s. Estimates of the prevalence of this arrhythmia in these studies vary greatly from country to country, but this variability should be treated with caution, as it may be the result of the methodologies used, particularly concerning the age of the subjects included, the lower limit of which ranges from 18 to 65 years.

Moreover, it is difficult to detect cases in the community, since diagnosis requires at least an electrocardiogram. For this reason, many studies are based on populations recruited at primary care centers and are therefore inevitably biased.

In the late 2000s, we found that there were no reliable data on the prevalence and incidence of AF in Portugal.

We considered this to be a significant deficiency, particularly given the high stroke-related mortality rate in Portugal and the known fact that AF is the cause of at least 15% of ischemic strokes.<sup>2</sup> We concluded that knowledge of these parameters for all ages would help improve AF control and hence stroke prevention, and this led to a wide-ranging epidemiological study aiming to provide an accurate overview of the situation in Portugal. This was the FAMA study, published in 2010.<sup>4</sup>

The FAMA study established a reference value for AF prevalence that has since received broad acceptance as representing the Portuguese population over 40 years of age. The study was designed to be highly rigorous in its enrollment criteria in order to avoid sample bias and to ensure that the sample was truly representative of the Portuguese population. To this end, the study was planned to cover populations from all over Portugal. Several municipalities were randomly selected in each geographical area, and several localities were chosen within each. The population sample was selected using random-route methods, which involved taking a predetermined route in each locality, starting from a previously established random starting point.<sup>5</sup>

Nevertheless, the FAMA study had the limitation of underestimating the actual prevalence of AF, since an unknown proportion of the population could have had paroxysmal AF that was not present at the time of performing the ECG. To obtain figures that are closer to reality, we would need more accurate knowledge of the prevalence of paroxysmal AF, for which the few available estimates vary considerably (35–60%).

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Almost eight years after the FAMA study, two new studies have attempted to overcome or at least diminish this limitation, by documenting more cases of paroxysmal AF through prolonged electrocardiographic monitoring. These are a recent study by Primo et al.<sup>6</sup> and the SAFIRA study, presented in this issue of the *Journal*.<sup>7</sup>

Twenty-four-hour Holter monitoring was used to identify patients with AF in all the patients in Primo et al. and in a randomized subset of 400 patients in the SAFIRA study. In the latter study, an additional 200 individuals were fitted with an event recorder for two weeks.

However, the need for a more complex and costly examination made it necessary to reduce the size of the population studied compared to the FAMA study, and made it impractical for these two studies to be carried out in the community. The consequent unavoidable selection process meant that these studies cannot be considered truly representative of the general population.

In the SAFIRA study, recruitment was performed partly at health centers, but mostly (93.7%) outside of these centers, through partnerships with civil society (charitable organizations, parish councils, senior centers and retirement homes). This reduced, but could not completely overcome, the selection bias of the population enrolled in the study.

The SAFIRA study was of an elderly population (aged 65 years or older), who were also included in the FAMA study. However, the population of the former could be analyzed in greater detail. The prevalence found for AF (9%) was higher than in the FAMA study, but for specific age-groups the difference was not so significant (there was no division at age 65 in the FAMA study, but prevalence between 70 and 80 years was 6.6%, and for  $\geq 80$  years it was 10.4%). These results are, as the authors point out, in agreement with those of two reference studies in other countries, the Rotterdam study<sup>8</sup> and a Spanish study by Cea-Calvo et al.<sup>9</sup> However, the prevalence was lower than that found by Primo et al.<sup>6</sup> (12.4%) in a population that was younger (over 40 years of age), but probably more selected and potentially more severe, since they were recruited at two reference centers for Holter monitoring.

Although almost a decade had passed since the FAMA study, the proportion of patients with unknown AF was still high – 35.9% in the SAFIRA study vs. 38% in the FAMA study. This indicates that, unfortunately, the public still has insufficient knowledge of this important arrhythmia.

Antithrombotic treatment standards were analyzed in detail in the SAFIRA study, the most important finding being that 56.3% of patients with previously known AF were not on oral anticoagulation therapy, compared to 37.8% in the FAMA study (29.8% of patients were on antiplatelet agents alone in the SAFIRA study, vs. 21.8% in the FAMA study). We can conclude that little progress has been made in the compliance of Portuguese physicians with international guidelines, which recommend anticoagulation therapy in the vast majority of AF patients. The older age of patients in the SAFIRA study partly explains this finding, but fear of bleeding complications should not inhibit physicians from using a therapy with such a favorable risk-benefit ratio. Worse still, analysis of CHA<sub>2</sub>DS<sub>2</sub>-VASc scores paradoxically showed lower anticoagulation rates (18.6%) in the groups with the highest scores (6 or more). Finally, the study found that even when

patients were medicated, this was inadequate: patients on vitamin K antagonists were receiving subtherapeutic doses most of the time (time in therapeutic range of only 41.7%), while among those taking new oral anticoagulants (NOACs) (around a third of those anticoagulated), a quarter were improperly medicated.

Despite some evidence of improvement following the introduction of NOACs, these findings certainly explain the high stroke rate found in patients enrolled in the study.

As is to be expected in this elderly population, the prevalence of cardiovascular risk factors was very high (hypertension 85.3%, dyslipidemia 75.4%, and diabetes 22.7%), substantially higher than in the FAMA study.

One of the reasons put forward by the authors to explain the higher prevalence of AF than in the FAMA study was that more cases of paroxysmal AF were included due to the use of Holter monitoring or an event recorder in some subjects. These methods did in fact lead to the detection of more cases of paroxysmal AF (in the SAFIRA study, three out of every five cases of paroxysmal AF detected [58/102] were detected by Holter monitoring or the event recorder). However, in total, the prevalence of this type of AF was only 18.6% of all patients with this arrhythmia, which is slightly lower than in the study by Primo et al.<sup>6</sup> (21.3%), in which Holter recording was used in all subjects. The authors point out that the decision to use the unweighted mean of the prevalences found in these subsets to calculate the prevalence in the overall sample was a limitation of this methodology, as it may have introduced a bias.

We believe that the differences between the studies are only partly explained by the inclusion of more cases of paroxysmal AF. As pointed out above, various factors related to enrollment can lead to the selection of subjects who are more severely ill and/or more prone to arrhythmias, as was the case of recruitment at Holter monitoring centers in the study by Primo et al.

The conclusions of the SAFIRA study reinforce and broaden those of the FAMA study, confirming the high prevalence of AF in the elderly Portuguese population and showing how, even after several years, problems such as the unsatisfactory rate of diagnosing this arrhythmia and the high proportion of patients not being prescribed anticoagulant therapy remain almost unchanged. We therefore agree with the authors on the need to identify and manage AF in this population and to optimize control of AF, stroke and systemic embolism, and of the importance of informing the public, patients, healthcare professionals and educators, as well as healthcare authorities, about the importance of this arrhythmia and the possibility of controlling symptoms and preventing complications. This will make it possible to achieve substantial health gains and to reduce morbidity and mortality.

## Conflicts of interest

The author has no conflicts of interest to declare.

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